

10/ 075,954

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAPLUS
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEADLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
NEWS 9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS 10	MAR 29	WPIFV now available on STN
NEWS 11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12	APR 26	PROMT: New display field available
NEWS 13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS 14	APR 26	LITALERT now available on STN
NEWS 15	APR 27	NLDB: New search and display fields available
NEWS 16	May 10	PROUSDDR now available on STN
NEWS 17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS 18	May 12	EXTEND option available in structure searching
NEWS 19	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS 20	May 17	FRFULL now available on STN
NEWS EXPRESS	MARCH 31	CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS		STN Operating Hours Plus Help Desk Availability
NEWS INTER		General Internet Information
NEWS LOGIN		Welcome Banner and News Items
NEWS PHONE		Direct Dial and Telecommunication Network Access to STN
NEWS WWW		CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 08:56:58 ON 25 MAY 2004

10/ 075,954

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 08:57:22 ON 25 MAY 2004

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STRUCTURE FILE UPDATES: 24 MAY 2004 HIGHEST RN 685504-43-2

DICTIONARY FILE UPDATES: 24 MAY 2004 HIGHEST RN 685504-43-2

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

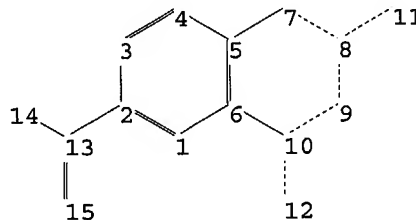
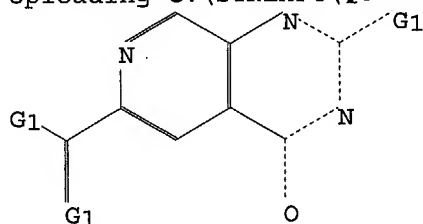
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

Uploading C:\STNEXP4\QUERIES\10075954.str



chain nodes :

11 12 13 14 15

ring nodes :

1 2 3 4 5 6 7 8 9 10

chain bonds :

2-13 8-11 10-12 13-14 13-15

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10

exact/norm bonds :

5-7 6-10 7-8 8-9 8-11 9-10 10-12 13-14 13-15

exact bonds :

2-13

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 :

G1:O,S,N

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS

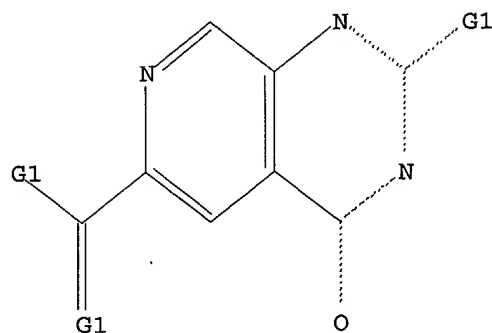
10/ 075,954

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1 ful

FULL SEARCH INITIATED 08:59:13 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 32 TO ITERATE

100.0% PROCESSED 32 ITERATIONS

15 ANSWERS

SEARCH TIME: 00.00.01

L2 15 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

156.26

156.47

FILE 'CAPLUS' ENTERED AT 08:59:20 ON 25 MAY 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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FILE COVERS 1907 - 25 May 2004 VOL 140 ISS 22

FILE LAST UPDATED: 24 May 2004 (20040524/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

10/ 075,954

=> s 12

L3 5 L2

=> d 13 1- ibib abs hitstr

YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:60320 CAPLUS

DOCUMENT NUMBER: 140:105336

TITLE: Combination of an allosteric carboxylic inhibitor of matrix metalloproteinase-13 with a selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use

INVENTOR(S): Roark, William Howard

PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA

SOURCE: PCT Int. Appl., 239 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006931	A2	20040122	WO 2003-IB3098	20030707

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004019054	A1	20040129	US 2003-619769	20030715
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PRIORITY APPLN. INFO.: US 2002-396785P P 20020717

OTHER SOURCE(S): MARPAT 140:105336

AB The invention provides a combination comprising an allosteric carboxylic inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with a selective inhibitor of COX-2, or a pharmaceutically acceptable salt thereof, that is not celecoxib or valdecoxib, and their use for the treatment of diseases that are responsive to inhibition of MMP-13 and cyclooxygenase-2.

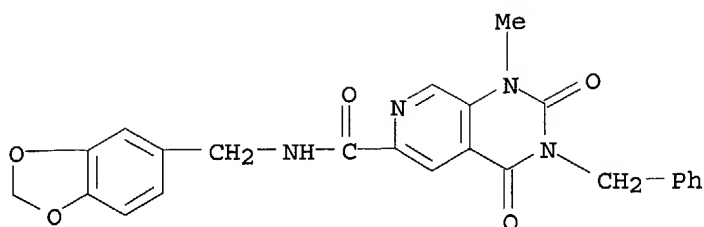
IT 449210-13-3 449210-20-2 449210-24-6
449210-27-9 449210-47-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

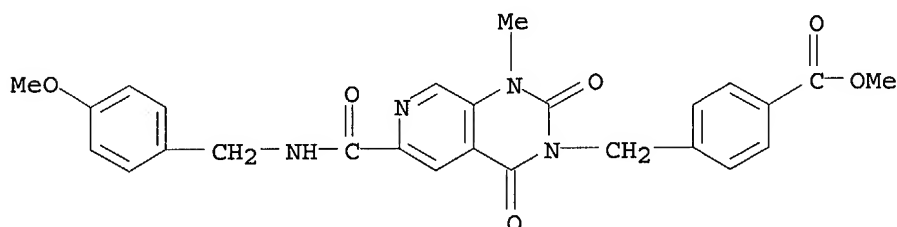
(allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use)

RN 449210-13-3 CAPLUS

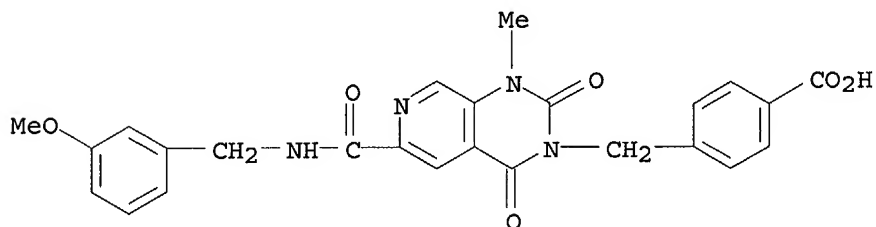
CN Pyrido[3,4-d]pyrimidine-6-carboxamide, N-(1,3-benzodioxol-5-ylmethyl)-1,2,3,4-tetrahydro-1-methyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



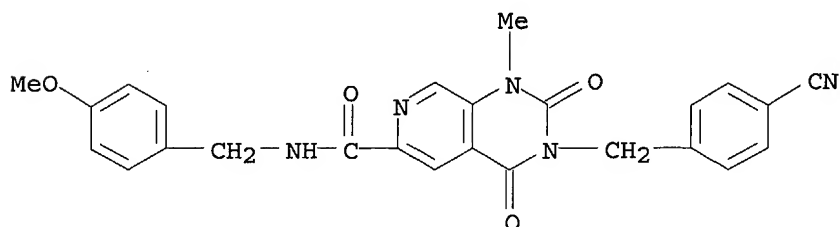
RN 449210-20-2 CAPLUS
 CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxypyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



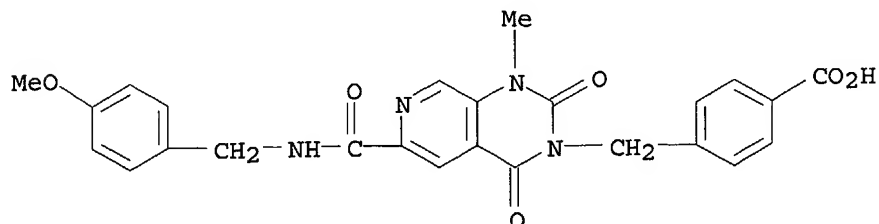
RN 449210-24-6 CAPLUS
 CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxypyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 449210-27-9 CAPLUS
 CN Pyrido[3,4-d]pyrimidine-6-carboxamide, 3-[(4-cyanophenyl)methyl]-1,2,3,4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)



RN 449210-47-3 CAPLUS
 CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxypyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:60302 CAPLUS

DOCUMENT NUMBER: 140:105333

TITLE: Combination of an allosteric carboxylic inhibitor of matrix metalloproteinase-13 with celecoxib or valdecoxib, pharmaceutical compositions, and therapeutic use

INVENTOR(S): Roark, William Howard

PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA

SOURCE: PCT Int. Appl., 238 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006912	A2	20040122	WO 2003-IB3044	20030707
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM</p> <p>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG</p>				

US 2004019053 A1 20040129 US 2003-619662 20030715

PRIORITY APPLN. INFO.: US 2002-396903P P 20020717

OTHER SOURCE(S): MARPAT 140:105333

AB The invention provides a combination comprising an allosteric carboxylic inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib, or a pharmaceutically acceptable salt thereof. The invention also provides a method of treating a disease that is responsive to inhibition of MMP-13 and cyclooxygenase 2, comprising administering to a patient suffering from such a disease the invention combination comprising an allosteric carboxylic inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib, or a pharmaceutically acceptable salt thereof. The invention also provides a pharmaceutical composition, comprising the invention combination comprising an allosteric carboxylic inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, or excipient. The invention combination may also be further combined with other pharmaceutical agents depending on the

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disease being treated.

IT 449210-13-3 449210-20-2 449210-24-6

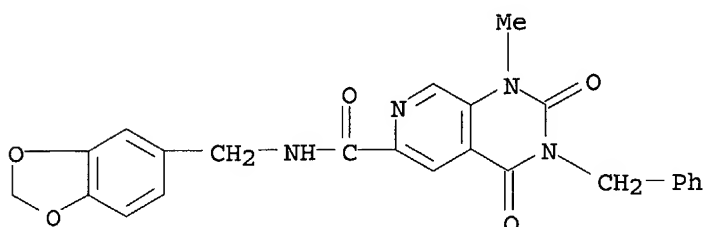
449210-27-9 449210-47-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(allosteric carboxylic inhibitor of matrix metalloproteinase-13
combination with celecoxib or valdecoxib, pharmaceutical compns., and
therapeutic use)

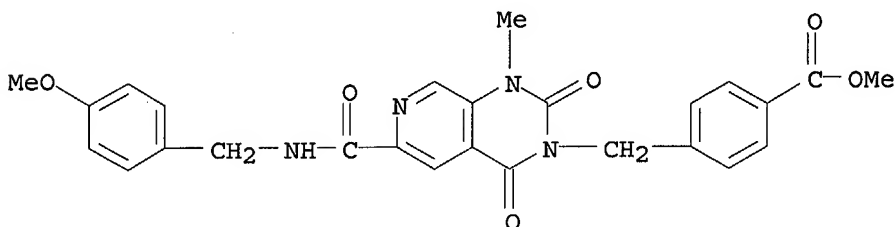
RN 449210-13-3 CAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxamide, N-(1,3-benzodioxol-5-ylmethyl)-
1,2,3,4-tetrahydro-1-methyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX
NAME)



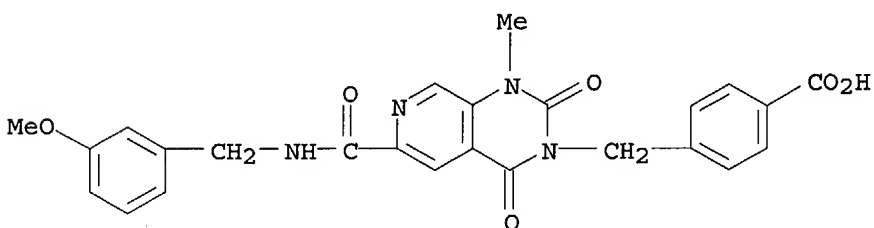
RN 449210-20-2 CAPLUS

CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-
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(9CI) (CA INDEX NAME)



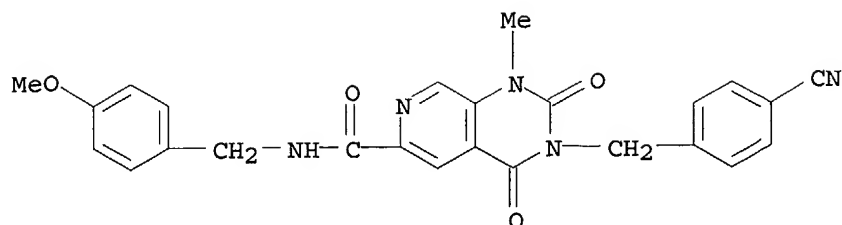
RN 449210-24-6 CAPLUS

CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]-
1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

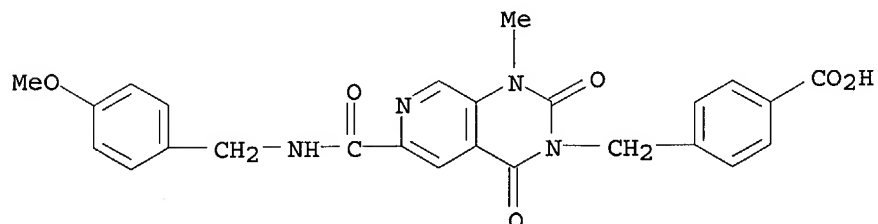


RN 449210-27-9 CAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxamide, 3-[(4-cyanophenyl)methyl]-1,2,3,4-
tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA
INDEX NAME)



RN 449210-47-3 CAPLUS
 CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxypyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA INDEX NAME)



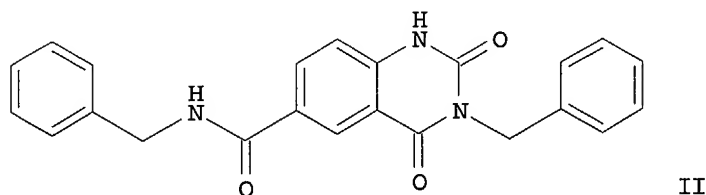
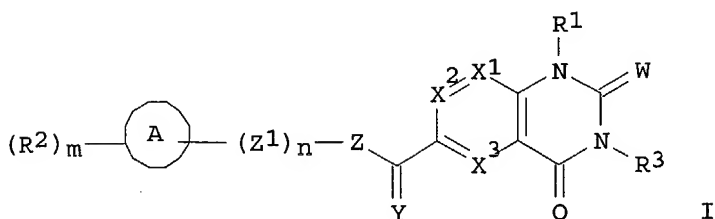
L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2002:637660 CAPLUS
 DOCUMENT NUMBER: 137:185501
 TITLE: Preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease
 INVENTOR(S): Andrianjara, Charles; Chantel-Barvian, Nicole; Gaudilliere, Bernard; Jacobelli, Henri; Ortwine, Daniel Fred; Patt, William Chester; Pham, Ly; Kostlan, Catherine Rose; Wilson, Michael William
 PATENT ASSIGNEE(S): Warner-Lambert Company, USA
 SOURCE: PCT Int. Appl., 264 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064572	A1	20020822	WO 2002-EP1979	20020211
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1368324	A1	20031210	EP 2002-722137	20020211
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
EE 200300384	A	20031215	EE 2003-384	20020211
US 2002193377	A1	20021219	US 2002-75954	20020213

Applicant

pregnant version

NO 2003003593 A 20030813 NO 2003-3593 20030813
 PRIORITY APPLN. INFO.: US 2001-268661P P 20010214
 WO 2002-EP1979 W 20020211
 OTHER SOURCE(S): MARPAT 137:185501
 GI



AB Title compds. I [R1 = H, amino, alkyl, alkenyl, alkynyl, alkylamino, aryl, heterocycle, etc.; W = O, S, =N-R'; R' = alkyl, OH, CN; X1-3 = N, C-R6; R6 = H, alkyl, amino, alkylamino, etc.; Y = O, S, NH, N-alkyl; Z = O, S, NR7; R7 = H, alkyl, aryl, aryl, heteroaryl, etc.; n = 1-8; Z1 = alkyl; A = (non)aromatic, 5- or 6-membered monocycle comprising from 0 to 4 heteroatoms selected from N, O, S, etc.; m = 0-7; R2 = alkyl, halo, CN, NO2, SCF3, CF3, OCF3, etc.; R3 = H, alkyl, alkenyl, alkynyl, etc.] were prepared Over 200 synthetic examples were provided. For instance, di-Me 4-aminoisophthalate was reacted with benzyllisocyanate and heated to 95-100° overnight to give Me 3-benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylate which was saponified (dioxaneaq, LiOH, reflux) to give the carboxylic acid. This intermediate was coupled with benzylamine to afford II. Selected examples of I had IC50 = 2.25 - 0.001 μM for MMP13 and IC50 > 100 μM for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12 and MMP14; II had IC50 = 0.193 μM for MMP13. Compds. I are useful for the treatment of osteoarthritis and rheumatoid arthritis.

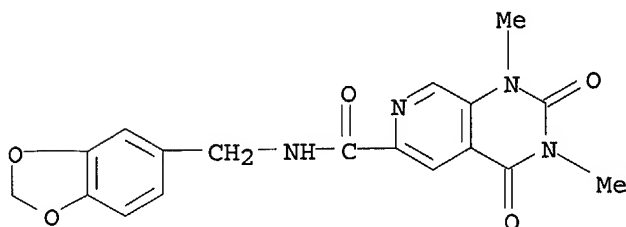
IT **449210-01-9P**, 1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide
449210-13-3P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide **449210-20-2P**, Methyl 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoate **449210-23-5P**, tert-Butyl 4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoate **449210-24-6P**, 4-[[6-(3-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoic acid **449210-27-9P**
449210-47-3P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoic acid
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(MMP13 inhibitor; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease)

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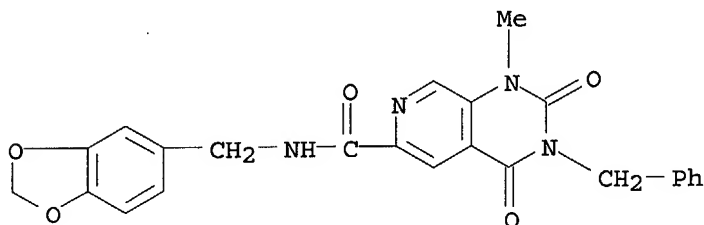
RN 449210-01-9 CAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxamide, N-(1,3-benzodioxol-5-ylmethyl)-
1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxo- (9CI) (CA INDEX NAME)



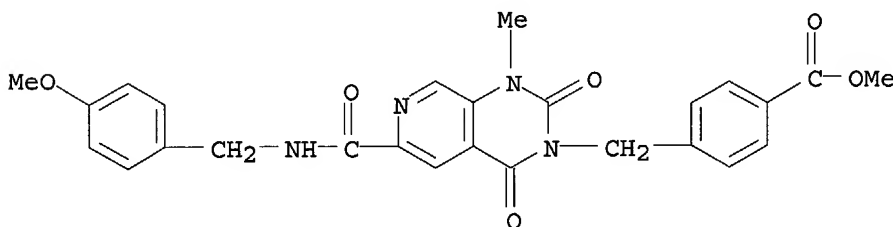
RN 449210-13-3 CAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxamide, N-(1,3-benzodioxol-5-ylmethyl)-
1,2,3,4-tetrahydro-1-methyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



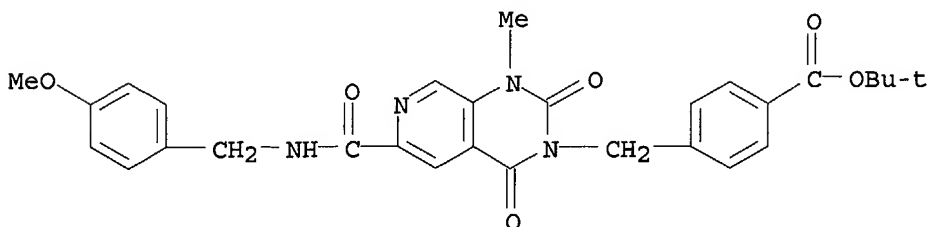
RN 449210-20-2 CAPLUS

CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-
1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester
(9CI) (CA INDEX NAME)



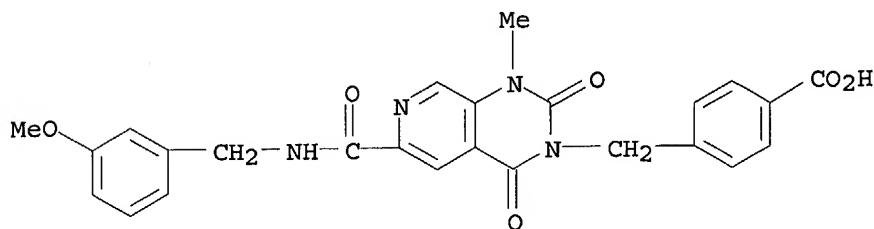
RN 449210-23-5 CAPLUS

CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-
1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-, 1,1-dimethylethyl ester
(9CI) (CA INDEX NAME)

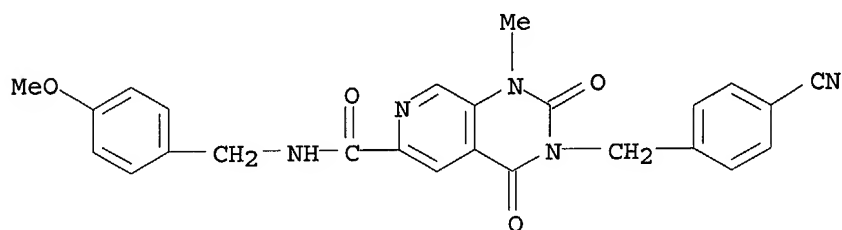


10/ 075,954

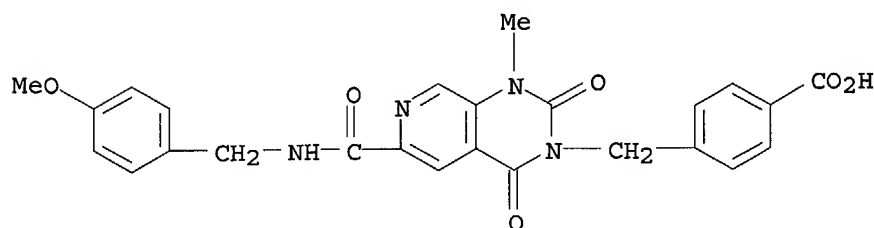
RN 449210-24-6 CAPLUS
CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxypyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)



RN 449210-27-9 CAPLUS
CN Pyrido[3,4-d]pyrimidine-6-carboxamide, 3-[(4-cyanophenyl)methyl]-1,2,3,4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA
INDEX NAME)



RN 449210-47-3 CAPLUS
CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxypyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

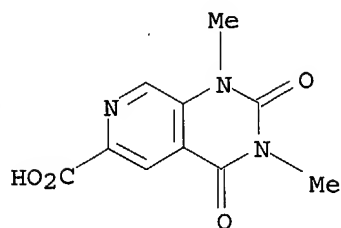


IT 449210-02-0P, 1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid 449210-18-8P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid methyl ester 449210-19-9P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid 449210-21-3P, 1-Methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid 449210-22-4P 449210-25-7P 449210-26-8P, tert-Butyl 4-[[[6-(3-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease)

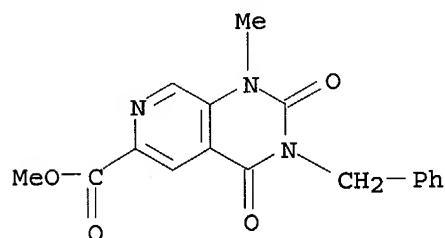
RN 449210-02-0 CAPLUS
CN Pyrido[3,4-d]pyrimidine-6-carboxylic acid, 1,2,3,4-tetrahydro-1,3-dimethyl-

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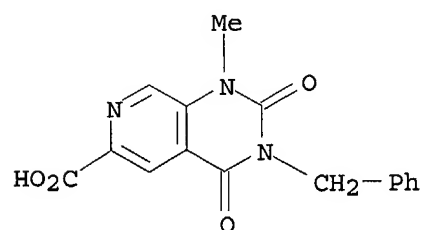
2,4-dioxo- (9CI) (CA INDEX NAME)



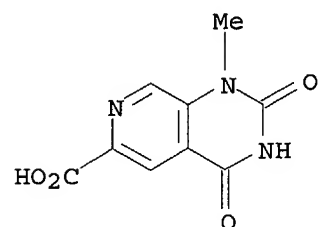
RN 449210-18-8 CAPLUS
CN Pyrido[3,4-d]pyrimidine-6-carboxylic acid, 1,2,3,4-tetrahydro-1-methyl-2,4-dioxo-3-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



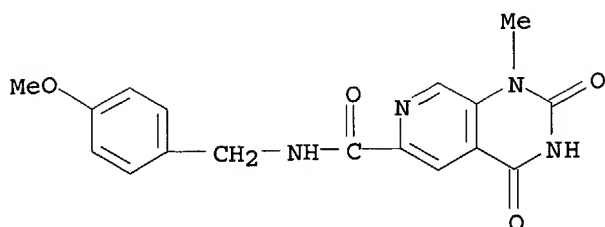
RN 449210-19-9 CAPLUS
CN Pyrido[3,4-d]pyrimidine-6-carboxylic acid, 1,2,3,4-tetrahydro-1-methyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



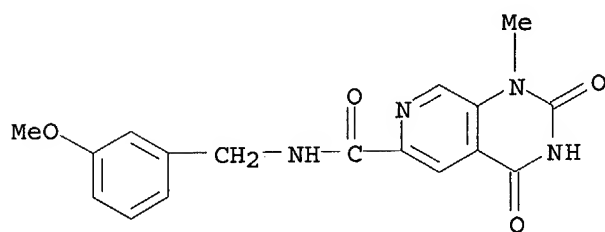
RN 449210-21-3 CAPLUS
CN Pyrido[3,4-d]pyrimidine-6-carboxylic acid, 1,2,3,4-tetrahydro-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)



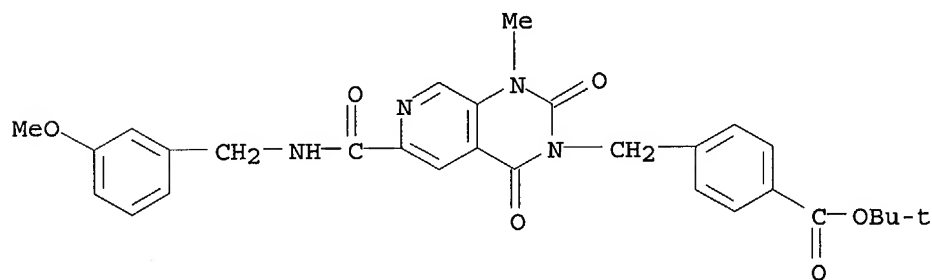
RN 449210-22-4 CAPLUS
CN Pyrido[3,4-d]pyrimidine-6-carboxamide, 1,2,3,4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)



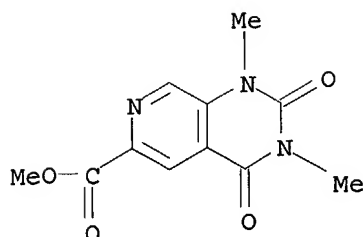
RN 449210-25-7 CAPLUS
 CN Pyrido[3,4-d]pyrimidine-6-carboxamide, 1,2,3,4-tetrahydro-N-[(3-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)



RN 449210-26-8 CAPLUS
 CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT 154470-79-8, Methyl 1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,4-d]pyrimidine-6-carboxylate
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactant; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease)
 RN 154470-79-8 CAPLUS
 CN Pyrido[3,4-d]pyrimidine-6-carboxylic acid, 1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxo-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:637472 CAPLUS

DOCUMENT NUMBER: 137:201321

TITLE: Preparation of substituted isophthalic acid derivatives, multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors

INVENTOR(S): Andrianjara, Charles; Ortwine, Daniel Fred; Pavlovsky, Alexander Gregory; Roark, William Howard

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 173 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

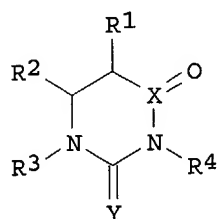
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

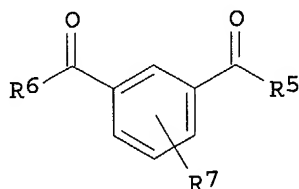
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064080	A2	20020822	WO 2002-IB447	20020213
WO 2002064080	A3	20021212		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003078276	A1	20030424	US 2002-75069	20020213
EP 1361873	A2	20031119	EP 2002-710275	20020213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002007864	A	20040309	BR 2002-7864	20020213
PRIORITY APPLN. INFO.:			US 2001-268821P	P 20010214 →
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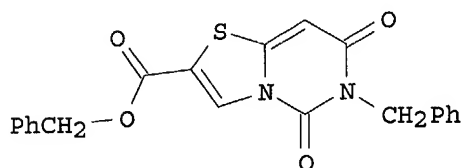
GI



I



II



III

AB Title compds., I [R1 and R2 together may form a substituted aromatic ring or a heterocyclic ring; or R2 and R3 together may form substituted heterocycle; or R1, R3, or R4 = alkyl, arylalkyl, etc.; X = C, S; Y = O, N with provision when Y = N it forms a 5-membered heterocycle with R3] and II [R5, R6 = arylalkylamine, heterocyclalkoxy, etc.; R7 = H, MeO, NO₂, etc.], are prepared and disclosed as matrix metalloproteinase (MMP) inhibitors. Thus, III was prepared in five steps via cyclocondensation of diethylmalonate and benzylurea with subsequent chlorination, substitution with hydrosulfide hydrate to form an in situ intermediate that was reacted with bromoacetaldehyde dimethylacetal, followed by acid catalyzed cyclization and substitution with benzylchloroformate. III was demonstrated to inhibit MMP13 with an IC₅₀ value (in μ M) of 0.0230. I and II bind allosterically to the catalytic domain of MMP-13 and comprise a hydrophobic group, first and second hydrogen bond acceptors and at least one, and preferably both, of a third hydrogen bond acceptor and a second hydrophobic group. Cartesian coordinates for centroids of the above features are defined in the specification. When the ligand binds to MMP-13, the first, second and third (when present) hydrogen bond acceptors bond resp. with Thr245, Thr247 and Met 253, the first hydrophobic group locates within the S1' channel of MMP-13 and the second hydrophobic group (when present) is relatively open to solvent. The compds. specifically inhibit the matrix metalloproteinase-13 enzyme and thus are useful for treating diseases resulting from tissue breakdown, such as heart disease, multiple sclerosis, arthritis, atherosclerosis, and osteoporosis.

IT 449210-18-8P 449210-19-9P 449210-21-3P

449210-22-4P

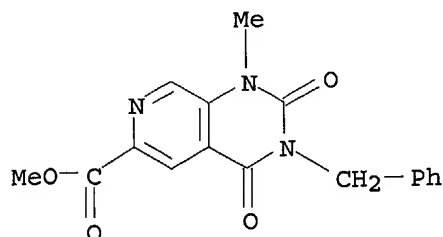
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

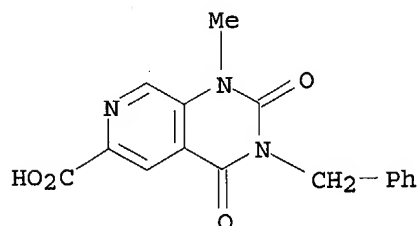
RN 449210-18-8 CAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxylic acid, 1,2,3,4-tetrahydro-1-methyl-2,4-dioxo-3-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)

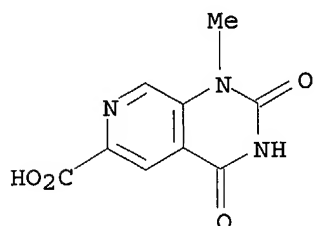
10/ 075,954



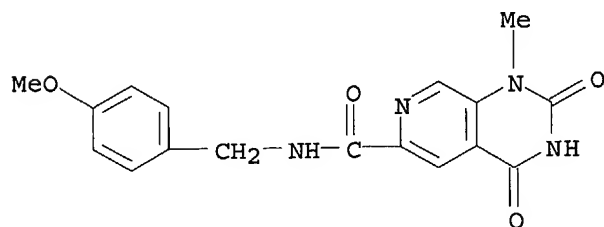
RN 449210-19-9 CAPLUS
CN Pyrido[3,4-d]pyrimidine-6-carboxylic acid, 1,2,3,4-tetrahydro-1-methyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 449210-21-3 CAPLUS
CN Pyrido[3,4-d]pyrimidine-6-carboxylic acid, 1,2,3,4-tetrahydro-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)



RN 449210-22-4 CAPLUS
CN Pyrido[3,4-d]pyrimidine-6-carboxamide, 1,2,3,4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)



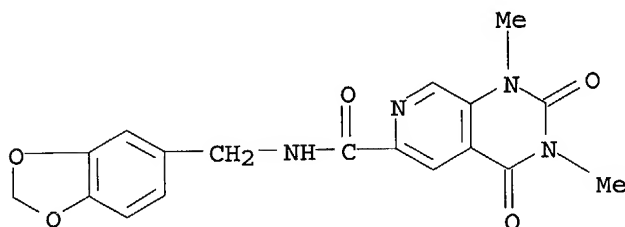
IT 449210-01-9P 449210-13-3P 449210-20-2P
449210-24-6P 449210-27-9P 449210-47-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(target compound; preparation and pharmaceutical activity of substituted

10/ 075,954

isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

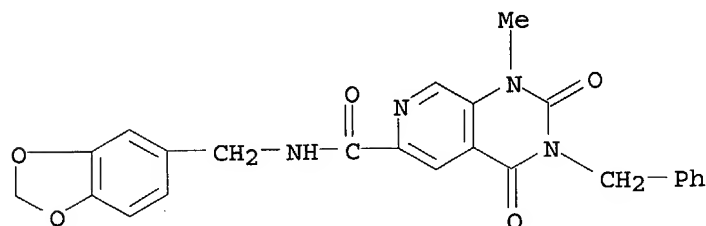
RN 449210-01-9 CAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxamide, N-(1,3-benzodioxol-5-ylmethyl)-1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxo- (9CI) (CA INDEX NAME)



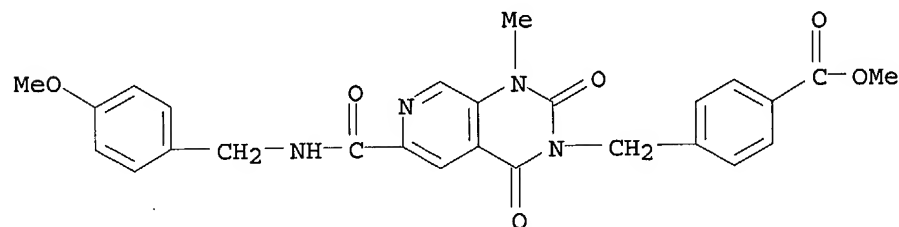
RN 449210-13-3 CAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxamide, N-(1,3-benzodioxol-5-ylmethyl)-1,2,3,4-tetrahydro-1-methyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



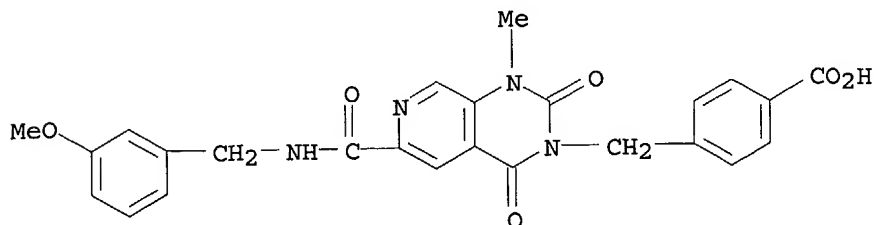
RN 449210-20-2 CAPLUS

CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

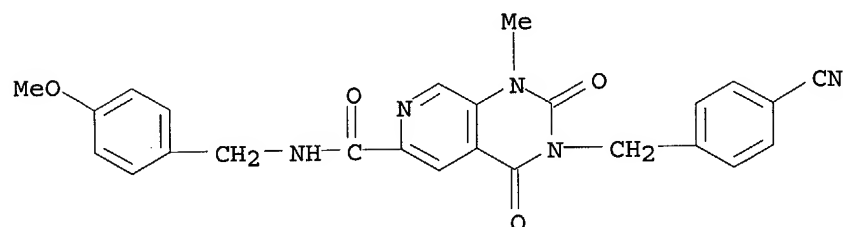


RN 449210-24-6 CAPLUS

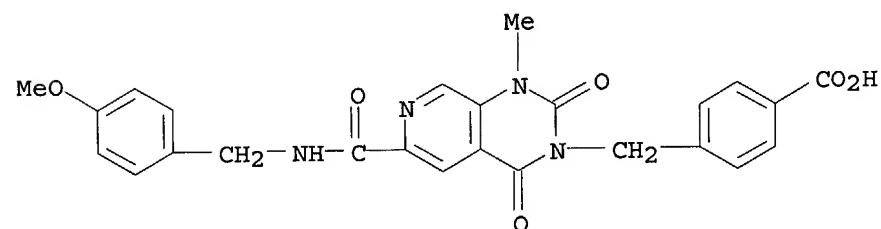
CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



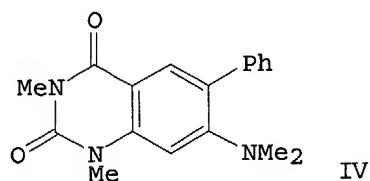
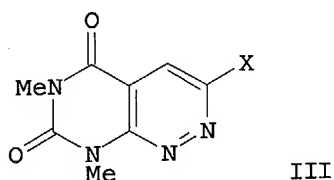
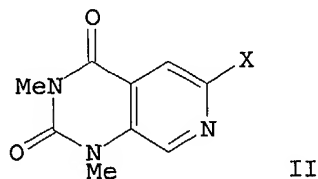
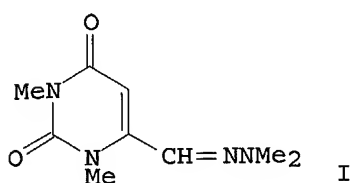
RN 449210-27-9 CAPLUS
 CN Pyrido[3,4-d]pyrimidine-6-carboxamide, 3-[(4-cyanophenyl)methyl]-1,2,3,4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)



RN 449210-47-3 CAPLUS
 CN Benzoic acid, 4-[[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA INDEX NAME)



L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1994:270302 CAPLUS
 DOCUMENT NUMBER: 120:270302
 TITLE: Novel synthesis of pyrido[3,4-d]pyrimidines, pyrido[2,3-d]pyrimidines, and quinazolines via palladium-catalyzed oxidative coupling
 AUTHOR(S): Hirota, Kosaku; Kuki, Hideki; Maki, Yoshifumi
 CORPORATE SOURCE: Gifu Pharm. Univ., Gifu, 502, Japan
 SOURCE: Heterocycles (1994), 37(1), 563-70
 CODEN: HTCYAM; ISSN: 0385-5414
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 120:270302
 GI



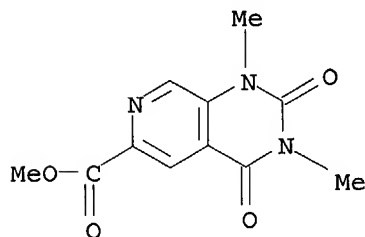
AB Oxidative-coupling of 6-azavinyl(or vinyl)-1,3-dimethyluracil derivs. (e.g. I) with electron-deficient olefins in the presence of palladium acetate led to the formation of the corresponding 6-substituted pyrido[3,4-d]pyrimidines (II, X = CO₂Me, CN, etc.), pyrido[2,3-d]pyrimidines (III, X = CN, Ac, etc.), and quinazolines (e.g. IV), resp., via intermediacy of an azatriene.

IT 154470-79-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 154470-79-8 CAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxylic acid, 1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxo-, methyl ester (9CI) (CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 08:56:58 ON 25 MAY 2004)

FILE 'REGISTRY' ENTERED AT 08:57:22 ON 25 MAY 2004

L1 STRUCTURE UPLOADED

L2 15 S L1 FUL

FILE 'CAPLUS' ENTERED AT 08:59:20 ON 25 MAY 2004

L3 5 S L2

=> log y

COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
24.22	180.69

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE ENTRY	TOTAL SESSION
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CA SUBSCRIBER PRICE

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-3.47

STN INTERNATIONAL LOGOFF AT 08:59:57 ON 25 MAY 2004